Appl. No. 09/939,230 Amdt. dated 2/24/2005 Reply to Office Action of August 25, 2004

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims

1-44. (Canceled)

- 45. (Original) A method for reducing anxiety in a subject in need thereof by increasing ion flow through KCNQ potassium channels in a cell, the method comprising the step of administering to the subject a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound able to increase ion flow through KCNQ potassium channels, said composition administered to the subject in a potassium channel-opening amount, thereby reducing anxiety in the subject.
- 46. (Original) The method of claim 45, wherein the anxiety is caused by panic disorder, generalized anxiety disorder, or stress disorder.
- 47. (Original) The method of claim 46, wherein the stress disorder is acute stress disorder or post-traumatic stress disorder.
 - 48. (Original) The method of claim 45, wherein the subject is a human.
- 49. (Original) The method of claim 45, wherein the KCNQ channel is a heteromeric channel.
- 50. (Original) The method of claim 45, wherein the KCNQ channel is a homomeric channel.
- 51. (Currently Amended) The method of claim 49 50, wherein the heteromeric KCNQ channel comprises a KCNQ2 polypeptide subunit.
- 52. (Currently Amended) The method of claim <u>49</u> 50, wherein the heteromeric KCNO channel comprises a KCNQ3 polypeptide subunit.

Appl. No. 09/939,230 Amdt. dated 2/24/05 Reply to Office Action of August 25, 2004

- 53. (Original) The method of claim 52, wherein the KCNQ channel is KCNQ2/3.
- 54. (Original) The method of claim 45, wherein the potassium channel-opening amount is 0.1 mg/kg to 200 mg/kg.
- 55. (Original) The method of claim 54, wherein the potassium channel-opening amount is 10 mg/kg to 100 mg/kg.
- 56. (Original) The method of claim 45, wherein the composition is administered orally.
- 57. (Original) The method of claim 45, wherein the composition is administered by injection.
- 58. (Original) The method of claim 45, wherein the compound able to increase ion flow through KCNQ potassium channels has the formula:

$$Ar^1$$
 N
 Ar^2

wherein

Ar¹ and Ar² are each members independently selected from the group consisting of aryl, substituted aryl, heteroaryl and substituted heteroaryl; and X is a member selected from the group consisting of O, S and N-R¹, wherein R¹ is a member selected from the group consisting of H, (C₁-C₈)alkyl, substituted (C₁-C₈)alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, aryl(C₁-C₄)alkyl, substituted aryl(C₁-C₄)alkyl, CN, -C(O)R², -OR³, -C(O)NR³R⁴, and -S(O)₂NR³R⁴;

- wherein R^2 is a member selected from the group consisting of (C_1-C_8) alkyl, substituted (C_1-C_8) alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, aryl (C_1-C_4) alkyl and substituted aryl (C_1-C_4) alkyl; and
- R³ and R⁴ are each members independently selected from the group consisting of hydrogen, (C₁-C₈)alkyl, substituted (C₁-C₈)alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, aryl(C₁-C₄)alkyl and substituted aryl(C₁-C₄)alkyl, or R³ and R⁴ can be combined with the nitrogen to which each is attached to form a 5-, 6- or 7-membered ring optionally having additional heteroatoms at the ring vertices.
- 59. (Currently Amended) The method according to claim 58, wherein Arl arl is a member selected from the group consisting of phenyl, substituted phenyl, indolyl, substituted indolyl, benzofuranyl, substituted benzofuranyl, furanyl, substituted furanyl, thienyl, substituted thienyl, isothiazolyl, substituted isothiazolyl, pyrazolyl and substituted pyrazolyl.
- 60. (Currently Amended) The method according to claim 58, wherein Arl is substituted phenyl, substituted or unsubstituted 2-indolyl and substituted or unsubstituted 2-thienyl.
 - 61. (Original) The method according to claim 58, wherein X is O.
- 62. (Original) The method according to claim 60, wherein the Ar¹ substituents are selected from the group consisting of halogen, alkyl, halo(C₁-C₄)alkyl, (C₁-C₄)alkoxy, halo(C₁-C₄)alkoxy, nitro, cyano, -NHC(O)R⁷, -NHR⁷, phenyl and substituted phenyl, wherein

 R^7 is a member selected from hydrogen, $(C_1\text{-}C_8)$ alkyl, substituted $(C_1\text{-}C_8)$ alkyl, cycloalkyl, substituted cycloalkyl, heteroalkyl, substituted heteroalkyl, heterocyclyl, substituted heterocyclyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, aryl $(C_1\text{-}C_4)$ alkyl and substituted aryl $(C_1\text{-}C_4)$ alkyl, or R^7 can be combined with the nitrogen to which it is attached to form a 5-, 6- or 7-membered ring optionally having additional heteroatoms at the ring vertices.

- 63. (Currently Amended) The method according to claim 58, wherein $\frac{Ar^2}{Ar^2}$ is selected from the group consisting of heteroaryl and substituted heteroaryl.
- 64. (Original) The method according to claim 58, wherein Ar¹ is substituted aryl; Ar² is heteroaryl or substituted heteroaryl; and X is O.
- 65. (Original) The method according to claim 62, wherein Ar² is pyridyl or substituted pyridyl.
- 66. (Original) The method according to claim 65, wherein Ar² is selected from the group consisting of 6-methyl-3-pyridyl and 2-chloro-5-pyridyl.
- 67. (Original) The method according to claim 65, wherein Ar¹ is substituted phenyl.
- 68. (Original) The method according to claim 67, said compound having the formula:

$$R^5$$

wherein,

Y is a member selected from the group consisting of halogen, C_1 - C_4 alkyl, C_1 - C_4 substituted alkyl, -OCH₃ and -OCF₃, and R^5 and R^6 are members independently selected from the group consisting of H, halogen, alkyl, halo(C_1 - C_4)alkyl, nitro, cyano and phenyl, with the proviso that both R^5 and R^6 are not H.

69. (Original) The method according to claim 68, wherein R⁵ and R⁶ are members independently selected from the group consisting of H, F, and Cl, with the proviso that both R⁵ and R⁶ are not H.

Appl. No. 09/939,230 Amdt. dated 2/24/05 Reply to Office Action of August 25, 2004

70. (Original) The method of claim 45, wherein the compound able to increase ion flow through KCNQ potassium channels has the formula:

wherein

- R¹ is a member selected from the group consisting of substituted or unsubstituted branched (C₃-C₈)alkyl, substituted or unsubstituted (C₃-C₈)cycloalkyl, substituted or unsubstituted or unsubstituted or unsubstituted or unsubstituted aryl and substituted or unsubstituted heteroaryl;
- R², R³, R⁴ and R⁵ are each members independently selected from the group consisting of hydrogen, fluorine and substituted or unsubstituted (C₁-C₈)alkyl, or optionally any two of R², R³, R⁴ and R⁵ are joined together to form a three- to seven-membered ring, having from 0 to 3 heteroatoms as ring members, or R² and R⁴ taken together form a second bond between the carbon atoms to which each is attached, or R², R³, R⁴ and R⁵ taken together represent a second and third bond between the carbon atoms to which each is attached;
- R⁶, R⁷, R⁸ and R⁹ are each members independently selected from the group consisting of hydrogen, fluorine and substituted or unsubstituted (C₁-C₈)alkyl, or optionally any two of R⁶, R⁷, R⁸ and R⁹ are joined together to form a three- to seven-membered ring, having from 0 to 3 heteroatoms as ring members;
- R¹⁰ is a member selected from the group consisting of substituted or unsubstituted (C₃-C₈)cycloalkyl, substituted or unsubstituted (C₃-C₈)heterocycloalkyl, substituted or unsubstituted aryl and substituted or unsubstituted heteroaryl;

X is a member selected from the group consisting of O, S and N-R¹¹, wherein R¹¹ is a member selected from the group consisting of H, (C₁-C₈)alkyl, substituted (C₁-C₈)alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, aryl(C₁-C₄)alkyl, substituted aryl(C₁-C₄)alkyl, -CN, -C(O)R¹², -OR¹³, -NR¹³R¹⁴, -C(O)NR¹³R¹⁴, and -S(O)₂NR¹³R¹⁴; wherein R¹² is a member selected from the group consisting of (C₁-C₈)alkyl, substituted (C₁-C₈)alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, aryl(C₁-C₄)alkyl and substituted aryl(C₁-C₄)alkyl; and

R¹³ and R¹⁴ are each members independently selected from the group consisting of hydrogen, (C₁-C₈)alkyl, substituted (C₁-C₈)alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, aryl(C₁-C₄)alkyl and substituted aryl(C₁-C₄)alkyl, or R¹³ and R¹⁴ can be combined with the nitrogen to which each is attached to form a 5-, 6- or 7-membered ring optionally having additional heteroatoms at the ring vertices; and

m, n, p and q are each independently an integer of from 0 to 1, with the proviso that at least one of m, n, p or q is 1.

- 71. (Original) The method of claim 70, wherein X of the compound is O.
- 72. (Original) The method of claim 70, wherein m and n of the compound are zero.
- 73. (Original) The method of claim 70, wherein m of the compound is 1 and n of the compound is zero.
- 74. (Original) The method of claim 70, wherein m and n of the compound are each 1.

Appl. No. 09/939,230 Amdt. dated 2/24/05 Reply to Office Action of August 25, 2004

- 75. (Original) The method of claim 70, wherein m and p of the compound are each zero, and n and q of the compound are each 1.
- 76. (Original) The method of claim 70, wherein m, n, p and q of the compound are each 1.
- 77. (Currently Amended) The method of claim 70, wherein R^2 and R^4 R2 and R4 of the compound, taken together, form a second bond joining the carbon atoms to which each is attached.
- 78. (Currently Amended) The method of claim 70, wherein m and p of the compound are each 1, R^2 , R^3 , R^6 and R^7 R2, R3, R6 and R7 of the compound are each hydrogen, n and q of the compound are each zero, and R^{10} R10 of the compound is selected from the group consisting of substituted or unsubstituted aryl and substituted or unsubstituted heteroaryl.
- 79. (Currently Amended) The method of claim 78, wherein $\frac{R^{10}}{R^{10}}$ of the compound is substituted aryl having from one to three substituents selected from the group consisting of halogen, halo(C1-C4)alkyl, halo(C1-C4)alkoxy, (C1-C4)alkyl, (C1-C4)alkoxy, nitro, cyano, phenyl and methylenedioxy.
- 80. (Currently Amended) The method of claim 70, wherein m, n, p and q of the compound are each 1, and R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^8 and R^9 of the compound are each hydrogen.
- 81. (Currently Amended) The method of claim 70, wherein m, n, p and q of the compound are each 1; R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^8 and R^9 R2, R3, R4, R5, R6, R7, R8 and R9 of the compound are each hydrogen; and R^{10} R10 of the compound is selected from the group consisting of substituted or unsubstituted aryl and substituted or unsubstituted heteroaryl.
- 82. (Currently Amended) The method of claim 81, wherein \underline{R}^1 R1 of the compound is selected from the group consisting of substituted or unsubstituted branched (C3-C8)alkyl, and substituted or unsubstituted (C3-C8)cycloalkyl.